REMARKS

Claims 71-92 are pending and active. Applicants herewith cancel claims 87 and 92, amend claim 72, and add new claims 93 and 94. No new matter is added with this amendment.

Support for new claim 93 can be found in the specification in Figurere 1c (see page 12, line 15 of the English translation of WO 97/34140). Claim 94, which is directed to the second embodiment claim 71, is supported in the specification at page 4, line 23 of the English translation.

I. Objections to the Claims

The Examiner has requested applicants to amend claim 75 to correct a typographical error. Applicants herewith comply with this request and respectfully ask the Examiner to withdraw this objection.

II. Rejections under 35 USC § 112

In paragraph 4, the Examiner rejects claim 72 under 35 USC § 112, second paragraph, for lack of clarity in reciting that the molecule is bound to "a surface of a gap." In response, applicants a herewith amend claim 72 to clarify that the gap is the area between two electrodes. Accordingly, applicants respectfully request withdrawal of this rejection.

III. Rejections under 35 USC § 103

The Examiner rejects claims 71 to 92 as being unpatentable over US Patent No. 6,020,110 (Williams *et al.*) in view of WO 93/22678 (Hollis *et al.*). According to the Examiner, Williams *et al.*, discloses manufacturing

and use of electrodes for the detection of nucleic acids, proteins and antibodies. The electrodes can be treated by bonding or absorption of enzymes as well as specific binding partners, for example DNA, avidin, biotin and so on. Applicants respectfully traverse this rejection.

Applicants assert that the Examiner's conclusions are based upon a misinterpretation of the art. For instance, the Examiner cites column 3, lines 5 to 6, alleging that this disclosure "teaches that the initial gap of the electrode is from 10 to 75 μm". However, the Examiner's wording deviates from that of Williams *et al.*, and, the electrode structures of Williams *et al.* differ from those of the present invention to such an extent that the word "gap," as used by the Examiner is something different from the "gap" as used in present claim 72.

Present claim 71 requires one to provide a single ultra-microelectrode array, said array comprising **at least 2 electrode structures**, wherein each of said electrode structures comprises a surface layer of conductive material, **is insulated from each other** and is either a layer on a planar insulating material or is incorporated in said planar insulating support material. **The space between the electrode structures** is about 1 μm or less to approaching this size of a large molecule complex. Thus, the relevant feature in the present invention is **the space between the electrode structures being about 1 μm or less.**

The electrodes for electrochemical sensing provided by Williams differ substantially from such an arrangement. As may be seen from figures 1 and 2, Williams provides a method for producing a microelectrode (see for example claim 1) which comprises depositing an electrically-conducting layer (2) on a suitable (plastic) substrate. Instead of structuring

this layer in order to obtain a microelectrode array comprising (more than one) electrode structures, this layer is superimposed by an electrically-insulating layer (3) of photoimagable dielectric material. An array of apertures that expose the conductive layer is formed in the insulating layer so that apertures (4) are provided. According to the description cited by the Examiner, *i.e.,* page 3, line 5, the diameter of the apertures may vary in the range 10 – 75 μm at regular spacing. A typical spacing will be apertures regularly spaced in the range 2 - 10 aperture diameters apart. This means that the width of each electrode (well) within the array of electrodes is in the range of 10-75 μm. The distance **between** two electrodes of the array is in the range of 20 to 750 μm (2 – 10 times the aperture diameter, *i.e.*, 2 – 10 times 10 – 75 μm). Thus, the expression "gap of the electrode" as used by the Examiner is neither an expression used by Williams *et al.*, nor does correspond to what is recited in the present claims. Instead, Williams uses an electrode array having electrodes which are separated from each other by at least a distance of 20 μm.

Further, Williams does not teach a single ultra-microelectrode array comprising **at least two electrode structures.** In contrast, the array consists of one structure only because the electrodes are defined by apertures in a covering layer which is deposited on **a continuous conducting layer.**

Moreover, the electrodes of Williams *et al.* are situated at the bottom of "wells". Thus, no "gaps" are situated between two electrodes of the electrode array; rather, they are separated by raised structures. Further, neighboring electrodes belong to the same electrode structure and **are not**

insulated from each other. In contrast, present claim 71 requires that each of the electrode structures is insulated from each other. Of course, a necessary consequence of this insulation is that if the electrode structures are a layer on a planar insulating support material, at least one of the electrode structures **must be structured**, because otherwise it would be impossible to provide **two electrode structures** in the single ultra-microelectrode array of present claim 71. This would also be the case if the electrode structures were arranged as a multi-layer structure (see claim 87) because even if the lower electrode structure would be provided as a continuous layer as seen in USP 6,020,110, the second structure would necessarily consist of a layer with at least gaps or hollows through which the first electrode structure would come into contact with the molecules of the liquid or gel.

In summary, Williams *et al.*, does not disclose the following features of present claim 71:

(a) the space between the electrode structures is about 1 μm or less to approaching the size of a large molecule complex;

(b) the electrodes are made of noble metals such as gold, or out of carbon;

(c) the ultra-microelectrode array consists of at least two electrode structures;

(d) said electrode structures are insulated from each other;

(e) each of the electrode structures is a **structures planar** layer on a planar insulating support material, or is incorporated in a **structure manner** in said planar insulating support material.

These differences are neither taught nor suggested by the cited art. Applicants note that the field of the present invention is crowded, with what appear to be small differences in structure making big differences in terms of function. In the absence to motivate the skilled artisan to make the changes noted above, the Examiner's rejection must fail. In that regard, the Examiner cites PCT publication WO 93/22678 ("Hollis") as providing motivation to arrange the electrodes such that the gap between the electrodes approximates the size of a large molecule complex, thereby rendering applicants' invention obvious. However, applicants again disagree with the Examiner's interpretation of this art.

In paragraph 14 of the Office Action, the Examiner says: "figure 1 depicts a device where the electrodes are arranged in a substantially planar manner as well as being stacked". This is not correct (see page 10, lines 1 to 14): the allegedly stacked electrode structure of figure 1 is the lead structure by which the electrodes are addressed. The optional resistor array is also depicted in figures 5A to 5D where it is shown that they are situated on a substrate 34. Page 10 describes that an optional resistor array of X and Y resistors 32 coupled to leads RX1, RX2, RX3...RXN and RY1, RY2, RY3...RYN (as shown in figure 1) are formed by metal evaporation or sputtering on substrate 34. After the resistors and the respective address lines have been formed, a SiO_2 film 50 is then formed by CVD on layer 32. A mask material is then formed on the SiO_2 film, for example by CVD (figure 5A). Openings 54, about two microns wide, are formed in the mask material layer 28 by photolithography and reactive ion etching (figure 5B). The next part of the SiO_2 layer is etched down to a deepness of about 4.000 Å (corresponding to 0.4 μm). The

upper and lower electrodes 21 and 20 are then formed by successive electron beam evaporation of the titanium layer followed by contact metallization with gold (reference numbers 26 and 16). Due to the lateral edges of the remaining mask material film 28, which serves as a precise self-aligning mask for defining the width of the fingers of lower electrode 20, the close spacing between the upper and lower electrodes without shorting is not possible (see page 11, lines 18 to 22).

Thus, figure 1 of Hollis *et al.* depicts a device where the electrodes are arranged in an interdigital manner of two electrode structures. However, such structures are neither arranged in a substantially planar manner, nor are they stacked. In contrast, the surface of the first electrode structure is about 4.500 Å below the surface of the second electrode structure (their thickness is almost identical, and the first structure is deposited in the well sites prepared by etching out about 4.000 Å SiO_2 plus 500 Å of the mask material). Indeed, an arrangement in a substantially planar manner **must necessarily be avoided** in order to avoid **shorting of the electrodes**. This is achieved in that the electrode thickness is about 2.300 Å (300 Å of Ti and 2.000 Å of Au) so that about 2.400 Å distance remains between the upper surface of the lower electrode structure and the lower edge of the upper electrode structure. Thus, the spacing between the upper and lower electrodes which, according to Hollis, "is of the order of the length (or diameter in solution) of the target DNA molecule" (and which is 2.200 Å, according to the description of the preparation in connection with figure 5) is a **vertical spacing**.

Applicants have previously pointed out the above distinctions and herewith incorporate such previous arguments(see Response filed January

9, 2003, page 12, last paragraph bridging lines 1 to 3 of page 13). Applicants believe that the Examiner previously found such arguments, which are also applicable to the presently amended claims, to be persuasive. Applicants therefore respectfully request reconsideration of the same.

Applicants assert that when the cited references are carefully read in their entirety, neither reference, alone or in combination, suggests or guides the skilled artisan toward the claimed invention. In view of these arguments and the above amendment, applicants respectfully request the Examiner to reconsider the rejection under 35 USC § 103.

CONCLUSION

Applicants respectfully request Examiner Sisson to consider the above remarks and enter the above amendment thereto. Early notification of allowance is earnestly requested. Examiner Sisson is encouraged to contact the undersigned attorney for applicants at 202-912-2142 for any reason related to the advancement of this case.

Respectfully submitted,

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